PATENT COOPERATION TREATY

From the:
INTERNATIONAL SEARCHING AUTHORITY

To:

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PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	3 FEB 2005
Applicant's or agent's file reference 13773739	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/AU2004/001689	3 December 2004	3 December 2003

International Patent Classification (IPC) or both national classification and IPC

Int. Cl. [7] C07D 213/74, 237/20, 239/42, 241/20, 253/07, 401/12, 401/14, 413/10, 403/10; A61K 31/4418, 31/444, 31/496, 31/497, 31/506, 31/53, 31/5377; A61P 29/00, 37/00

Applicant

CYTOPIA RESEARCH PTY LTD et al

1. This opinion contains indications relating to the following items:

[X]	Box No. I	Basis of the opinion
[ ]	Box No. II	Priority
[ ]	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
[ ]	Box No. IV	Lack of unity of invention
[X]	Box No. V	Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
[X]	Box No. VI	Certain documents cited
[X]	Box No. VII	Certain defects in the international application
[X]	Box No. VIII	Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the IPEA/AU	Authorized Officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	**L.F. MCCAFFERY** Telephone No. (02) 6283 2573

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Box No. I Basis of the opinion

1. With regard to the **language,** this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☐ in computer readable form

   c. time of filing/furnishing

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	**1-4, 11, 13, 16**	**YES**
	Claims	**5-10, 12, 14, 15, 17, 18**	**NO**
Inventive step (IS)	Claims	**1-4, 11, 13, 16**	**YES**
	Claims	**5-10, 12, 14, 15, 17, 18**	**NO**
Industrial applicability (IA)	Claims	**1-18**	**YES**
	Claims		**NO**

2. Citations and explanations:

The following documents are cited in this opinion:

D1 WO 2004/052868 (CYTOPIA PTY. LTD.) 24 June 2004

D2 WO 2003/099796 (CYTOPIA PTY. LTD.) 4 December 2003

D3 WO 2003/031406 (IRM LLC) 17 April 2003

D4 WO 2003/026661 (YAMANOUCHI PHARMACEUTICAL CO. LTD.) 3 April 2003

D5 WO 2002/060492 (CYTOPIA PTY. LTD.) 8 August 2002

Novelty

Current claims 1-4 are limited to the use of the defined compounds in a method of modulating microtubules, so that whilst there are disclosures of the compounds of the independent claim 1 in D3-D5, there is no suggestion of their effect on microtubules. The use of such compounds in modulating microtubule polymerisation is however disclosed in D1 (see Box VI Certain documents cited).

D3 discloses heterocyclic scaffolds within the scope of current claims 5 and 10. Use of the compounds as kinase inhibitors is disclosed (see p. 3, lines 10-23) as well as pharmaceutical formulations comprising said compounds (p. 33, line 8 – p. 36, line 16) so that claims 14 and 18 are also not novel.

Examples from D4 fall within the scope of current claims 7, 8 and 10 thus depriving these claims of novelty but are disclosed as effective in the treatment of insulin-related diseases and obesity, so that the dependent claims to methods of treatment (claims 14-18) are novel with respect to this document.

D5 discloses specific compounds which are within the scope of current claims 5, 7 and 8. The generic preparative method on p. 24-25 of D5 combined with the range of substituents exemplified in Examples 1-7 and Tables 4 and 5 further provides an enabling disclosure for compounds within the scope of claims 5-9 and 12. These compounds are disclosed as inhibitors of protein tyrosine kinases useful in the treatment of cancer and auto-immune diseases. Methods of use and compositions are described therefore also depriving claims 14, 15, 17 and 18 of novelty.

Inventive Step

Claims 5-10, 12, 14, 15, 17 and 18 are not inventive in the light of document D5. Although there are no specific disclosures of the pyridyl compounds of current claim 10 in D5, there is a generic disclosure so that it would be obvious to the skilled addressee to prepare such compounds to solve the current problem. The compounds of D5, which overlap with those of the current invention, are claimed as inhibitors of JAK. Methods of treating JAK-associated disease states are also claimed, with a number of these diseases listed in Tables 1 and 2, as well as a role in treating some autoimmune diseases (p. 4, lines 3-8). As one of the uses of the compounds of the current invention is the same as that for D5, and there is no unexpected result arising from the selected compounds of the current invention, the listed claims do not involve an inventive step.

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Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
P,X WO 2004/052868 (D1)	24 June 2004	11 December 2003	11 December 2002
P,X WO 2003/099796 (D2)	4 December 2003	23 May 2003	23 May 2002

WO 2004/052868 discloses specific compounds within the scope of claims 1, 5, 7 and 8 of the current application (see Table 1). There is also a generic disclosure of compounds within the scope of claims 2, 6, 9 and 12. The generic preparative method on p. 21-24 combined with the compounds exemplified in Table 1 provides an enabling disclosure for the compounds of claims 1, 2, 5-9 and 12. Claims 5-9 and 12 are not limited, being to compounds per se and are therefore anticipated by D1. The compounds of the prior art document are capable of binding to tubulin and are therefore useful in the modulation of microtubule polymerisation, so that claims 1 and 2 which are limited to this use are anticipated by D1. The compounds of the prior art are additionally disclosed as useful in the treatment of hyperproliferation disorders including cancer, depriving the dependent claims 3 and 4 of novelty. In addition, pharmaceutical compositions comprising these compounds, and their use in methods of suppressing cancer and other proliferative diseases including psoriasis (hyperproliferation) and inflammatory diseases are also indicated (see page 13, lines 1-12), therefore anticipating claims 14-18.

There is overlap with the generic definitions of Formulae I and II of WO 2003/099796 with Formulae II, III, IV and V of current claims 5, 7, 8 and 10, with a specific disclosure of a compound within the scope of claim 5. The disclosed compound is, however, not within the scope of the invention of the prior art due to the proviso that when Y is $NHCOCH_3$, then R2 is 1-2 substituents. The generic synthetic method described on p. 19-21 combined with the examples and the compounds listed in Table 1 of this prior art document is considered to be enabling, so that claims 5-10 and 12 are not novel. Compositions comprising a carrier and at least one compound and methods of treating hyperproliferation disorders and protein-kinase related disorders using said compositions are disclosed, so that claims 14, 15, 17 and 18 also lack novelty.

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

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Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

There are two claims numbered 17 and two claims numbered 18.

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim 4 is not clear in its appendency to claim 2 as there is no mention of hyperproliferation-related disorder or disease state in claim 2.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V

Industrial Applicability

The subject matter of all the claims is considered to be industrially applicable.

See Box VI Certain documents cited for a discussion of the relevance of D1 and D2.